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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,143	SHAH ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the Appeal Brief filed on August 15, 2007, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing at the end of this Action.

Claims 1-18 are pending. Claim 18 is withdrawn. Claims 1-17 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-10 and claims 11-18 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-10 recite the phrase "predefined, desired functionality". The metes and bounds of this phrase in the context of the above claims are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. Therefore, it is not clear to the Examiner either from the specification or from the claim as to what specific "functions" of glucose oxidases are encompassed in the phrase "predefined, desired functionalities". Examiner requests clarification of the above term.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the specification on page 12, paragraph [0038], describes an example of a "desired functionality" and therefore, the claims are not indefinite. Examiner respectfully disagrees. The specification on page 12, paragraph [0038], does not provide a specific definition for the phrase, but only gives one example of a "predefined, desired functionality". Therefore, the metes and bounds of the functionalities encompassed by the above phrase are not clear.

Hence the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Cherry et al. and Hatzinikolaou et al.

Claims 1-3, 7-14 and 17 are drawn to a method of formulating glucose oxidases by obtaining an organism, such as an *E. coli*, with glucose oxidase genes, growing colonies of the organism, altering the environment of the colonies, such as introducing peroxide, screening the colonies to identify colonies with active glucose oxidase for a predefined, desired functionality, such as use in glucose sensors, and determining whether the colonies grown in the presence of peroxide are active.

Valdes et al. (cited previously on form PTO-892) discloses that glucose oxidase in glucose sensors are degraded by peroxide and this "decay can lead to the eventual failure of the senor" (abstract and page 367). Valdes et al. teaches that to ensure longer sensor functionality, instead of replacing the sensor with fresh enzyme, as has been practiced in the art, techniques to "prevent the degradation of the enzyme" is advantageous (page 375). With this teaching at hand, one having ordinary skill in the art would conclude that glucose oxidase may be prevented by using chemical agents, as suggested by Valdes et al. or to use glucose oxidase mutants that are resistant to peroxide since methods of generating mutants having resistance to chemicals are known in the art, as discussed below. Valdes et al. also teaches a method of determining activity of glucose oxidase (page 370.

The difference between the reference of Valdes et al. and the instant invention is that the reference of Valdes et al. does not teach a method of producing mutant glucose oxidase that is resistant to degradation from peroxide. However, there are many methods widely available in the art of creating mutant genes by random mutations and screening for mutants displaying desired functional properties, such as having resistance to a chemical, such as a peroxide.

Cherry et al. (Nat Biotechnol. 1999 Apr;17(4):379-84 - form PTO-892) discloses a method of making mutants of an enzyme which is also degraded in the presence of hydrogen peroxide by using directed evolution techniques, both DNA shuffling and error prone PCR (abstract). Cherry et al. discloses that after multiple rounds of directed evolution an enzyme, mutants of said enzyme that are resistant to deactivation in the

presence of high concentration of hydrogen peroxide, conditions that mimic of hydrogen peroxide wherein the enzyme is normally deactivated, were obtained (pages 380-382). Cherry et al. discloses that colonies having enzymatic activity were selected to determine for its resistance against hydrogen peroxide (page 382).

Hatzinikolaou et al. (cited previously on form PTO-892) discloses a library of glucose oxidase genes known in the art, such as *A. Niger* (page 371). Hatzinikolaou et al. also discloses a method of isolating and purifying glucose oxidase as recited in claims 10-14 and 17 and methods of measuring glucose oxidase activity and concentration of glucose oxidase (pages 372-373).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al., it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to apply the method of Cherry et al. to formulate or produce mutant glucose oxidases having resistance to peroxide by generating a library of mutated genes using the glucose oxidase gene of Hatzinikolaou et al., transforming *E. coli* with vectors comprising each of the mutated genes, growing colonies of said cells and determining whether the colonies have active glucose oxidase followed by determining whether the colonies or the glucose oxidase comprised in the colony are resistant to peroxide and then test for the functionality of the glucose oxidase in a glucose sensor. One of ordinary skill in the art would have been motivated to produce mutant peroxide resistant glucose oxidases in order to use them in glucose sensors, thereby prolonging their use, since Valdes et al. teaches that glucose oxidases in glucose sensors are degraded by peroxide, leading to failure of the sensor. One of

ordinary skill in the art would have had a reasonable expectation of success since Hatzinikolaou et al. teaches glucose oxidase genes and Cherry et al. teaches a comparable method of generating a library of mutant having resistance to hydrogen peroxide. Therefore, using the known technique of Cherry et al. to generate mutants of an enzyme having resistance against hydrogen peroxide would have been obvious to one of ordinary skill in the art.

Therefore, the above references render claims 1-3, 7-14 and 17 *prima facie* obvious.

Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Cherry et al. and Hatzinikolaou et al. as applied to claims, 1-3, 7-14 and 17 above, and further in view of MIXONIX.

Claims 15-16 are drawn to a method of formulating or producing mutant glucose oxidases, wherein colonies comprising said mutant glucose oxidase is disrupted via sonication.

Valdes et al., Cherry et al. and Hatzinikolaou et al. in combination teaches a method of formulating or producing mutant glucose oxidases, as discussed above.

The difference between the reference of Valdes et al., Cherry et al. and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of disrupting cells via sonication.

However, disrupting cells via sonication, through the use of a sonicator, during protein purification is well known and routinely practiced in the art, see MISONIX (form PTO-892).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al. and MISONIX, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to disrupt cells comprising mutant glucose oxidase via sonication. One of ordinary skill in the art would have been motivated to do so in order to disrupt cells comprising the mutant glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since disruption of cells using sonication is well known and practiced routinely in the art.

Therefore, the above references render claims 15-16 *prima facie* obvious.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Cherry et al. and Hatzinikolaou et al. as applied to claims 1-3, 7-14 and 17 above, and further in view of Wagner and Aldrich Catalog.

Claims 4-6 are drawn to a method of formulating or producing mutant glucose oxidases by obtaining a library of glucose oxidase genes, creating a library of mutated glucose oxidase genes, introducing each mutated glucose oxidase genes into separate expression vectors, inserting said vectors into host organisms, growing colonies of the host organism, determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence of a leuco-cryalsta-violet, and determining whether the colonies are resistant to peroxide.

Valdes et al., Cherry et al. and Hatzinikolaou et al. in combination teaches a method of formulating or producing mutant glucose oxidases, as discussed above.

The difference between the reference of Valdes et al., Cherry et al. and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence.

Wagner (EP 0 251 475 A1 – cited previously on form PTO-892) discloses a method of determining glucose oxidase activity via a sensor by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission (pages 2-3). In the method of Wagner, the glucose oxidase is conjugated to a dye and immobilized in the sensor (page 3). Wagner also teaches that any fluorescent dye sensitive to quenching of its fluorescence emission by oxygen can be used (page 5). Aldrich Catalog (cited previously on form PTO-892) discloses a leuco-cryalsta-violet dye (page 1005).

Therefore, combining the teachings of Valdes et al., Cherry et al. and Hatzinikolaou et al., Wagner and Aldrich Catalog, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the method of Wagner to ascertain activity of the glucose oxidase, wherein glucose oxidase is isolated and purified by the method taught by Hatzinikolaou et al. One of ordinary skill in the art would have been motivated to do so in order to determine whether the colonies comprising mutated glucose oxidases have active glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since

Wagner teaches how to determine activity of glucose oxidase by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission.

Therefore, the above references render claims 4-6 *prima facie* obvious.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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